STIC Search Report
EIC 1700

STIC Database Tracking Number: 164458

TO: Ben Sackey **Location: REM 5C18** **Art Unit : 1626** **September 20, 2005** **Case Serial Number: 10/650358**	**From: Kathleen Fuller** **Location: EIC 1700** **REMSEN 4B28** **Phone: 571/272-2505** **Kathleen.Fuller@uspto.gov**

Search Notes

FOR OFFICIAL USE ONLY

ACCESS DB # 164458

PLEASE PRINT CLEARLY

Scientific and Technical Information Center

SEARCH REQUEST FORM

Requester's Full Name: BEN SACKEY Examiner #: 73489 Date: 8/30/05

Art Unit: 1626 Phone Number: 2-0704 Serial Number: 10/650,358

Location (Bldg/Room#): Rm 5B31 Mailbox #: 5C-16 Results Format Preferred (circle): PAPER / DISK

To ensure an efficient and quality search, please attach a copy of the cover sheet, claims, and abstract or fill out the following:

Title of Invention: Tetrazolylpropionamides as Inhibitors of Abeta Protein Production

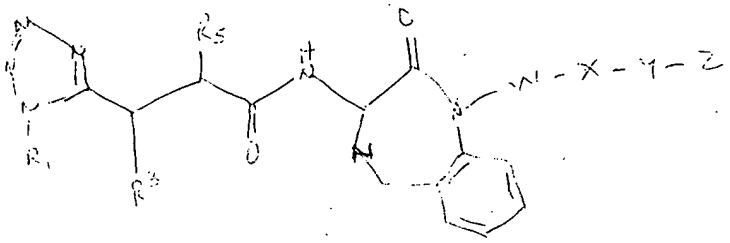
Inventors (please provide full names): Michael G. Yang

Earliest Priority Date: 5/27/02

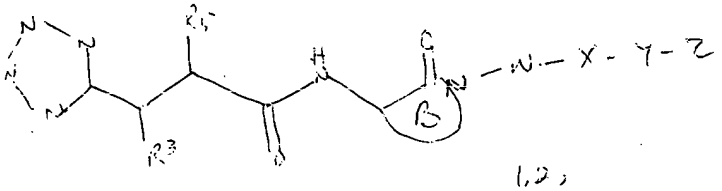
Search Topic:

Please provide a detailed statement of the search topic, and describe as specifically as possible the subject matter to be searched. Include the elected species or structures, keywords, synonyms, acronyms, and registry numbers, and combine with the concept or utility of the invention. Define any terms that may have a special meaning. Give examples or relevant citations, authors, etc., if known.

For Sequence Searches Only *Please include all pertinent information (parent, child, divisional, or issued patent numbers) along with the appropriate serial number.*



Elected Species is Compound # 38



B has been restricted to 1,4 or 1,5 diazepin

1,2,

Thanks

STAFF USE ONLY

Searcher: K. Fuller

Searcher Phone #:

Searcher Location:

Date Searcher Picked Up:

Date Completed: 9/20/05

Searcher Prep & Review Time: 20

Online Time: 15

Type of Search

___ NA Sequence (#)

___ AA Sequence (#)

1 Structure (#)

___ Bibliographic

___ Litigation

___ Fulltext

___ Other

Vendors and cost where applicable

✓ STN ___ Dialog

___ Questel/Orbit ___ Lexis/Nexis

___ Westlaw ___ WWW/Internet

___ In-house sequence systems

___ Commercial ___ Oligomer ___ Score/Length

___ Interference ___ SPDI ___ Encode/Transl

___ Other (specify)

=> FILE REG
FILE 'REGISTRY' ENTERED AT 18:04:03 ON 20 SEP 2005

Property values tagged with IC are from the ZIC/VINITI data file provided by InfoChem.

STRUCTURE FILE UPDATES: 19 SEP 2005 HIGHEST RN 863478-08-4
DICTIONARY FILE UPDATES: 19 SEP 2005 HIGHEST RN 863478-08-4

New CAS Information Use Policies, enter HELP USAGETERMS for details.

TSCA INFORMATION NOW CURRENT THROUGH JULY 14, 2005

Please note that search-term pricing does apply when conducting SmartSELECT searches.

****
* *
* The CA roles and document type information have been removed from *
* the IDE default display format and the ED field has been added, *
* effective March 20, 2005. A new display format, IDERL, is now *
* available and contains the CA role and document type information. *
* *
****

Structure search iteration limits have been increased. See HELP SLIMITS for details.

Experimental and calculated property data are now available. For more information enter HELP PROP at an arrow prompt in the file or refer to the file summary sheet on the web at:
http://www.cas.org/ONLINE/DBSS/registryss.html

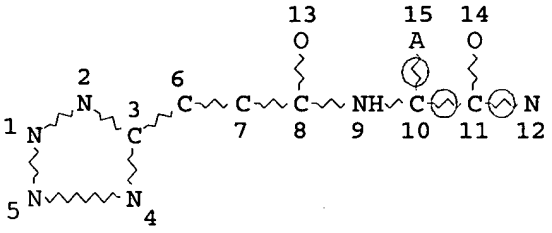
=> FILE HCAPL
FILE 'HCAPLUS' ENTERED AT 18:04:07 ON 20 SEP 2005

FILE COVERS 1907 - 20 Sep 2005 VOL 143 ISS 13
FILE LAST UPDATED: 19 Sep 2005 (20050919/ED)

New CAS Information Use Policies, enter HELP USAGETERMS for details.

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> D QUE
L12 STR



22 structures from the query

NODE ATTRIBUTES:
NSPEC IS R AT 10
NSPEC IS R AT 11
NSPEC IS R AT 12
NSPEC IS R AT 15
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 15

STEREO ATTRIBUTES: NONE
L14 22 SEA FILE=REGISTRY SSS FUL L12
L16 2 SEA FILE=HCAPLUS ABB=ON L14

2 CA references

=> D L16 BIB ABS IND HITSTR 1-2

L16 ANSWER 1 OF 2 HCAPLUS COPYRIGHT 2005 ACS on STN
AN 2004:354682 HCAPLUS
DN 140:375195
TI Tetrazolylpropionamides as inhibitors of Aβ protein production
IN Yang, Michael G.
PA USA
SO U.S. Pat. Appl. Publ., 52 pp.
CODEN: USXXCO
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 2004082568	A1	20040429	US 2003-650358	20030827
PRAI	US 2002-406144P	P	20020827		

applicant

OS MARPAT 140:375195
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Title compds. I [R1 = H, alk(en/yn)yl; R3, R5 = H, amino, alk(en/yn)yl, etc.; R3a, R5a = H, alk(en)yl, etc.; R6 = H, alkyl; B = 7-membered lactam, etc.; W = bond, CH2, CH2CH2; X = bond, Ph, pyridyl, etc.; Y = bond, CO, O, S, etc.; Z = H, alk(en/yn)yl, etc.] are prepared For example, (R)-4-methyl-2-((1-propyl-1H-tetrazol-5-yl)methyl)pentanoic acid (preparation

given) is coupled to a substituted benzodiazepine (DMF, HATu, i-Pr2NEt) to give II. Compds. of the invention exhibit IC50 < 10 μM for γ-secretase. I inhibit the processing of amyloid precursor protein and, more specifically, inhibit the production of Aβ-peptide, thereby acting to prevent the formation of neurol. deposits of amyloid protein. I are useful for the treatment of neurol. disorders related to β-amyloid production, such as Alzheimer's disease and Down's Syndrome.

IC ICM A61K031-55
ICS A61K031-454; C07D043-02; A61K031-41

INCL 514217090; 514326000; 514381000; 540603000; 546210000; 548252000

CC 28-21 (Heterocyclic Compounds (More Than One Hetero Atom))
Section cross-reference(s): 1, 34, 63

ST tetrazolylpropionamide inhibitor A protein prodn prepn; benzodiazepinone prepn amyloid precursor protein inhibitor; lactam prepn Alzheimers disease Downs syndrome treatment

IT Alzheimer's disease
Anti-Alzheimer's agents
Human
(preparation of benzodiazepinones as inhibitors of Aβ production for treatment of Alzheimer's disease and Down's syndrome)

IT Down's syndrome
(treatment; preparation of benzodiazepinones as inhibitors of Aβ production for treatment of Alzheimer's disease and Down's syndrome)

IT Amyloid
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(β-; preparation of benzodiazepinones as inhibitors of Aβ production for treatment of Alzheimer's disease and Down's syndrome)

IT 338454-52-7, γ-Secretase
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(preparation of benzodiazepinones as inhibitors of Aβ production for treatment of Alzheimer's disease and Down's syndrome)

IT **682812-71-1P**
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation of benzodiazepinones as inhibitors of Aβ production for treatment of Alzheimer's disease and Down's syndrome)

IT **682812-67-5P 682812-68-6P 682812-69-7P**
682812-70-0P 682812-72-2P 682812-73-3P
682812-74-4P 682812-75-5P 682812-76-6P
682813-00-9P 682813-01-0P 682813-02-1P
682813-03-2P 682813-04-3P 682813-05-4P
682813-06-5P 682813-07-6P 682813-08-7P
682813-09-8P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of benzodiazepinones as inhibitors of Aβ production for treatment of Alzheimer's disease and Down's syndrome)

IT 60-34-4, Methylhydrazine 75-26-3, Isopropyl bromide 106-95-6, Allyl bromide, reactions 107-10-8, Propylamine, reactions 1489-69-6, Cyclopropylcarboxaldehyde 1493-27-2, 2-Fluoronitrobenzene 1723-55-3 7051-34-5 36982-84-0, Trisyl azide 73259-81-1 120301-10-2 124676-19-3 130165-76-3 148415-75-2 280568-66-3 682812-96-0 682812-97-1 682812-98-2 682812-99-3
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of benzodiazepinones as inhibitors of Aβ production for treatment of Alzheimer's disease and Down's syndrome)

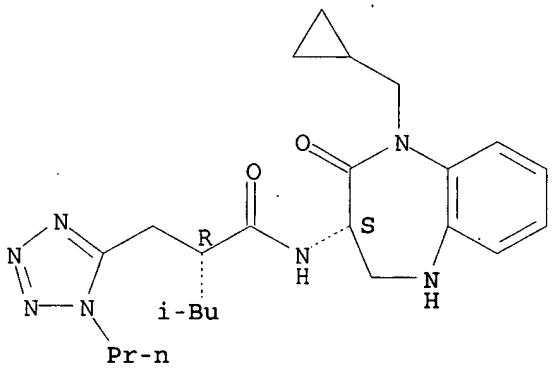
IT 790-10-3P 175211-37-7P 175211-38-8P 175211-39-9P 400819-99-0P 400820-00-0P 682812-77-7P 682812-78-8P 682812-79-9P 682812-80-2P

682812-81-3P 682812-82-4P 682812-84-6P 682812-85-7P 682812-86-8P
682812-87-9P 682812-88-0P 682812-90-4P 682812-91-5P 682812-92-6P
682812-93-7P 682812-94-8P 682812-95-9P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of benzodiazepinones as inhibitors of Aβ production for treatment of Alzheimer's disease and Down's syndrome)

IT **682812-71-1P**
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation of benzodiazepinones as inhibitors of Aβ production for treatment of Alzheimer's disease and Down's syndrome)

RN 682812-71-1 HCAPLUS
CN 1H-Tetrazole-5-propanamide, N-[(3S)-1-(cyclopropylmethyl)-2,3,4,5-tetrahydro-2-oxo-1H-1,5-benzodiazepin-3-yl]-α-(2-methylpropyl)-1-propyl-, (αR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT **682812-67-5P 682812-68-6P 682812-69-7P**
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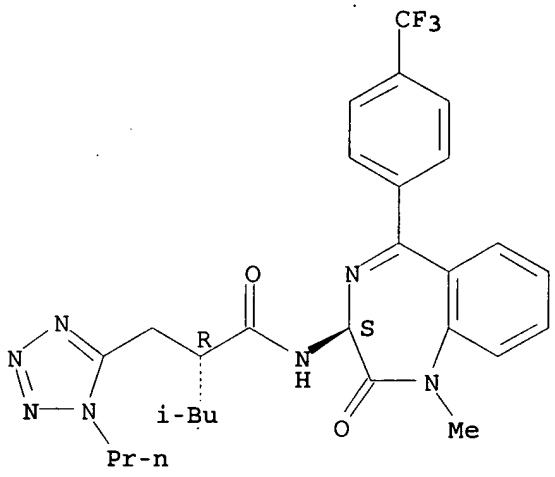
682812-74-4P 682812-75-5P 682812-76-6P
682813-00-9P 682813-01-0P 682813-02-1P
682813-03-2P 682813-04-3P 682813-05-4P
682813-06-5P 682813-07-6P 682813-08-7P
682813-09-8P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of benzodiazepinones as inhibitors of Aβ production for treatment of Alzheimer's disease and Down's syndrome)

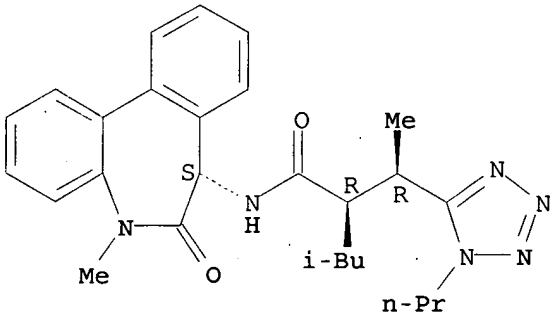
RN 682812-67-5 HCAPLUS
CN 1H-Tetrazole-5-propanamide, N-[(3S)-2,3-dihydro-1-methyl-2-oxo-5-[4-(trifluoromethyl)phenyl]-1H-1,4-benzodiazepin-3-yl]-α-(2-methylpropyl)-1-propyl-, (αR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



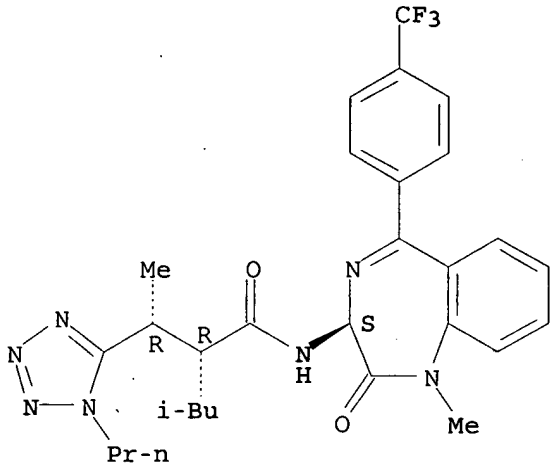
RN 682812-68-6 HCAPLUS
CN 1H-Tetrazole-5-propanamide, N-[(7S)-6,7-dihydro-5-methyl-6-oxo-5H-dibenz[b,d]azepin-7-yl]-β-methyl-α-(2-methylpropyl)-1-propyl-, (αR,βR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



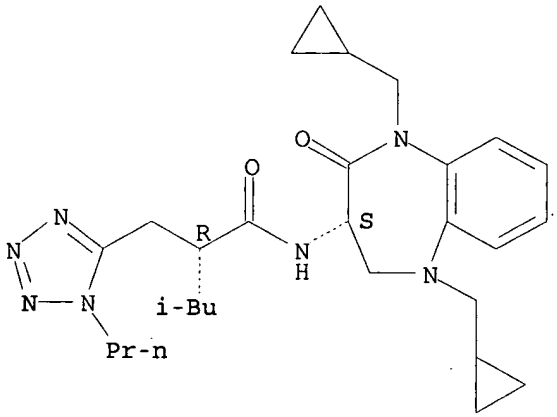
RN 682812-69-7 HCAPLUS
CN 1H-Tetrazole-5-propanamide, N-[(3S)-2,3-dihydro-1-methyl-2-oxo-5-[4-(trifluoromethyl)phenyl]-1H-1,4-benzodiazepin-3-yl]-β-methyl-α-(2-methylpropyl)-1-propyl-, (αR,βR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



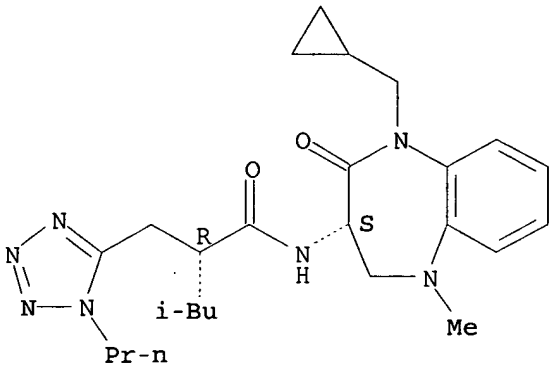
RN 682812-70-0 HCAPLUS
CN 1H-Tetrazole-5-propanamide, N-[(3S)-1,5-bis(cyclopropylmethyl)-2,3,4,5-tetrahydro-2-oxo-1H-1,5-benzodiazepin-3-yl]-α-(2-methylpropyl)-1-propyl-, (αR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 682812-72-2 HCAPLUS
CN 1H-Tetrazole-5-propanamide, N-[(3S)-1-(cyclopropylmethyl)-2,3,4,5-tetrahydro-5-methyl-2-oxo-1H-1,5-benzodiazepin-3-yl]-α-(2-methylpropyl)-1-propyl-, (αR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



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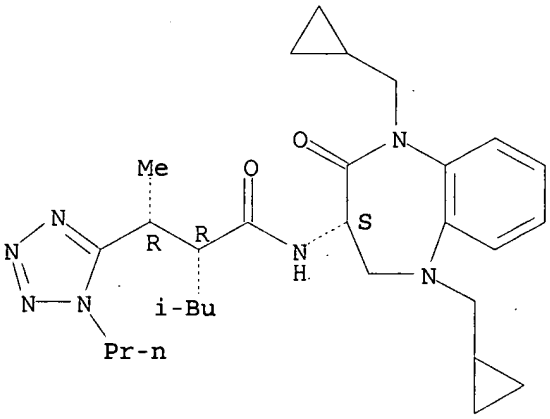
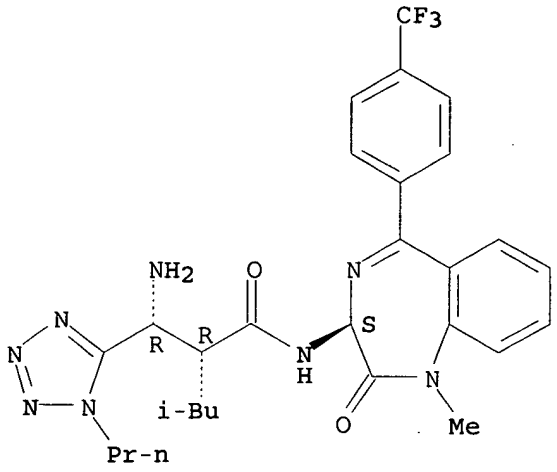
CN 1H-Tetrazole-5-propanamide, N-[(3S)-1,5-bis(cyclopropylmethyl)-2,3,4,5-tetrahydro-2-oxo-1H-1,5-benzodiazepin-3-yl]-β-methyl-α-(2-methylpropyl)-1-propyl-, (αR,βR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



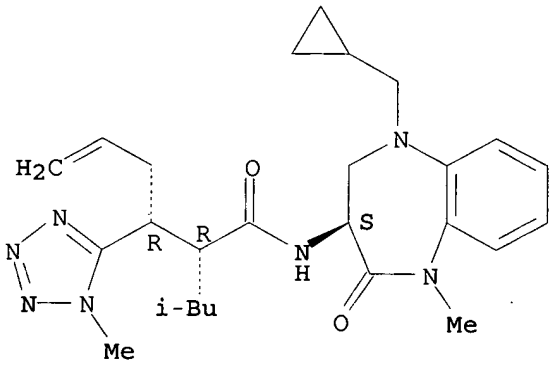
RN 682812-74-4 HCAPLUS
CN 1H-Tetrazole-5-propanamide, β-amino-N-[(3S)-2,3-dihydro-1-methyl-2-oxo-5-[4-(trifluoromethyl)phenyl]-1H-1,4-benzodiazepin-3-yl]-α-(2-methylpropyl)-1-propyl-, (αR,βR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 682812-75-5 HCAPLUS
CN 1H-Tetrazole-5-propanamide, N-[(3S)-5-(cyclopropylmethyl)-2,3,4,5-tetrahydro-1-methyl-2-oxo-1H-1,5-benzodiazepin-3-yl]-1-methyl-α-(2-methylpropyl)-β-2-propenyl-, (αR,βR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



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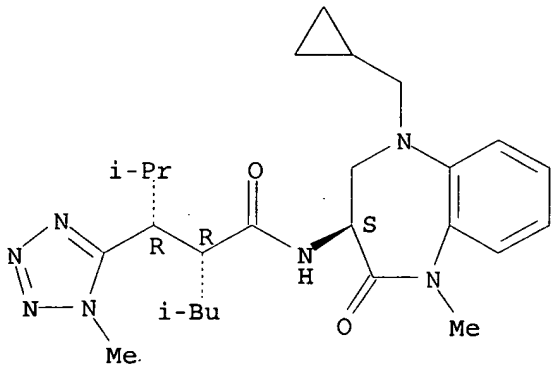
Absolute stereochemistry.



RN 682813-00-9 HCAPLUS
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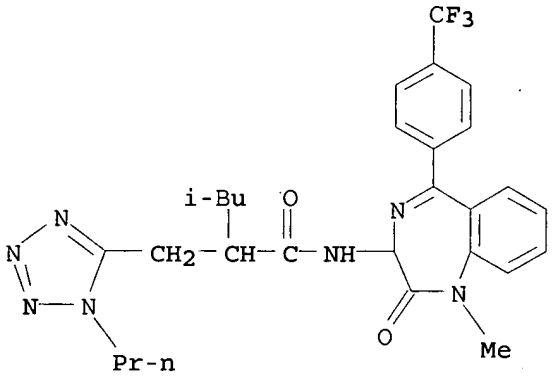
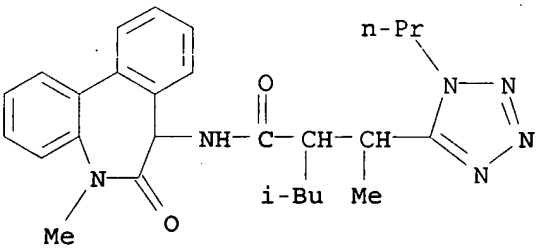


RN 682813-01-0 HCAPLUS
CN 1H-Tetrazole-5-propanamide, N-(6,7-dihydro-5-methyl-6-oxo-5H-dibenz[b,d]azepin-7-yl)-β-methyl-α-(2-methylpropyl)-1-propyl- (9CI) (CA INDEX NAME)



RN 682813-02-1 HCAPLUS
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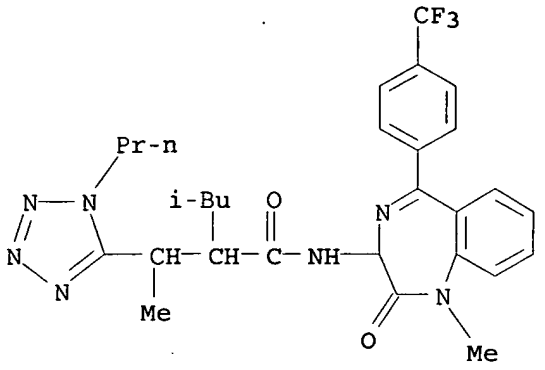

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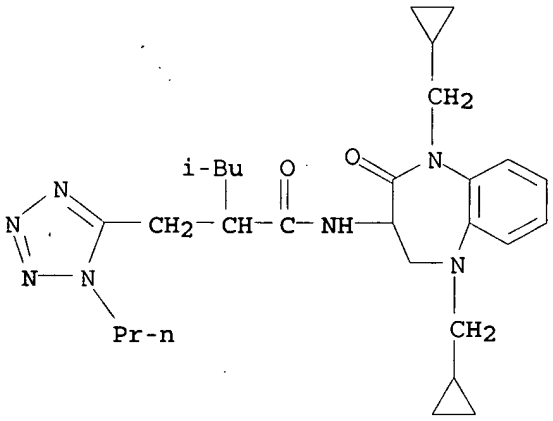
CN 1H-Tetrazole-5-propanamide, N-[1,5-bis(cyclopropylmethyl)-2,3,4,5-tetrahydro-2-oxo-1H-1,5-benzodiazepin-3-yl]-α-(2-methylpropyl)-1-propyl- (9CI) (CA INDEX NAME)



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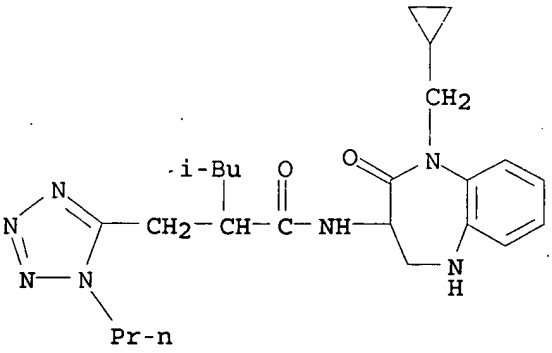

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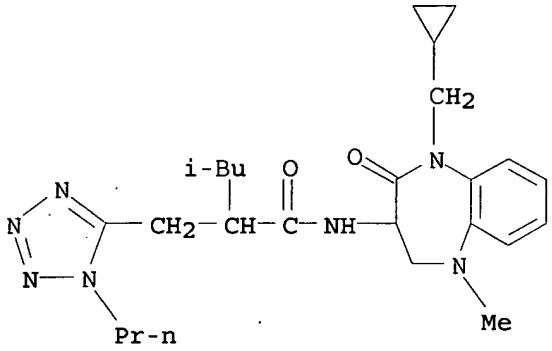
methyl-2-oxo-1H-1,5-benzodiazepin-3-yl]-α-(2-methylpropyl)-1-propyl- (9CI) (CA INDEX NAME)



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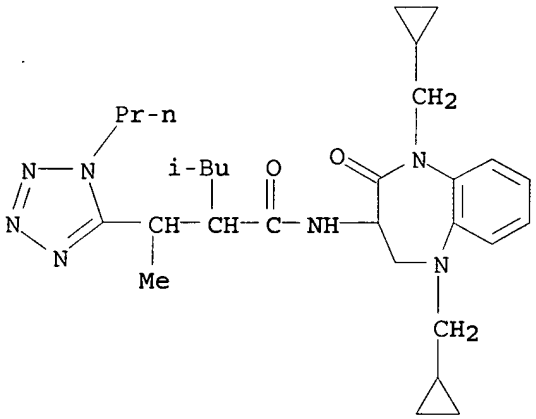

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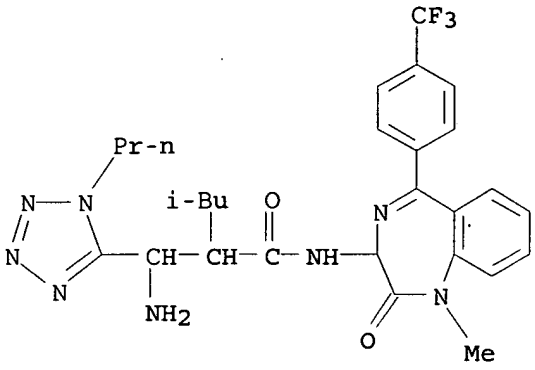
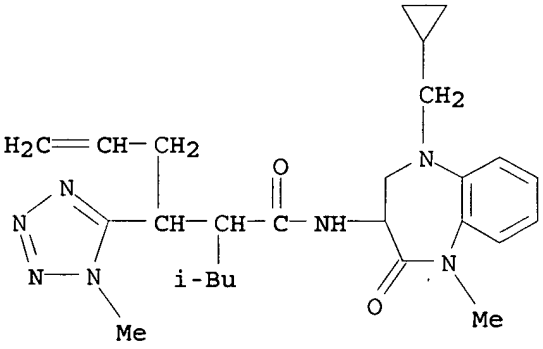
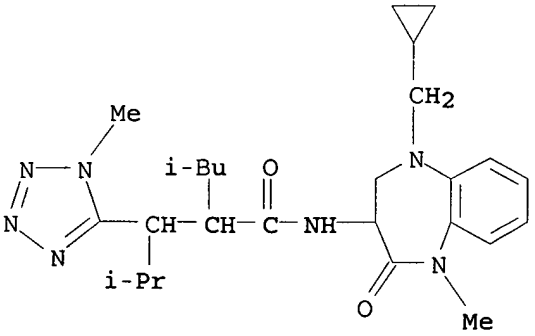


RN 682813-08-7 HCAPLUS
CN 1H-Tetrazole-5-propanamide, N-[5-(cyclopropylmethyl)-2,3,4,5-tetrahydro-1-methyl-2-oxo-1H-1,5-benzodiazepin-3-yl]-1-methyl-α-(2-methylpropyl)-β-2-propenyl- (9CI) (CA INDEX NAME)



RN 682813-09-8 HCAPLUS
CN 1H-Tetrazole-5-propanamide, N-[5-(cyclopropylmethyl)-2,3,4,5-tetrahydro-1-methyl-2-oxo-1H-1,5-benzodiazepin-3-yl]-1-methyl-β-(1-methylethyl)-α-(2-methylpropyl)- (9CI) (CA INDEX NAME)



L16 ANSWER 2 OF 2 HCAPLUS COPYRIGHT 2005 ACS on STN
AN 1988:221491 HCAPLUS
DN 108:221491

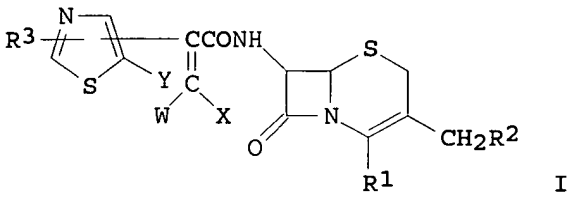
TI Preparation of alkenylcarboxamidocephemcarboxylic acid derivatives as antibiotics

IN Takatani, Takao; Sakane, Kazuo; Yamanaka, Hideaki; Matsuo, Teruaki
PA Fujisawa Pharmaceutical Co., Ltd., Japan

SO Jpn. Kokai Tokkyo Koho, 23 pp.
CODEN: JKXXAF
DT Patent
LA Japanese
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	JP 62215593	A2	19870922	JP 1986-58860	19860317
PRAI	JP 1986-58860		19860317		

GI



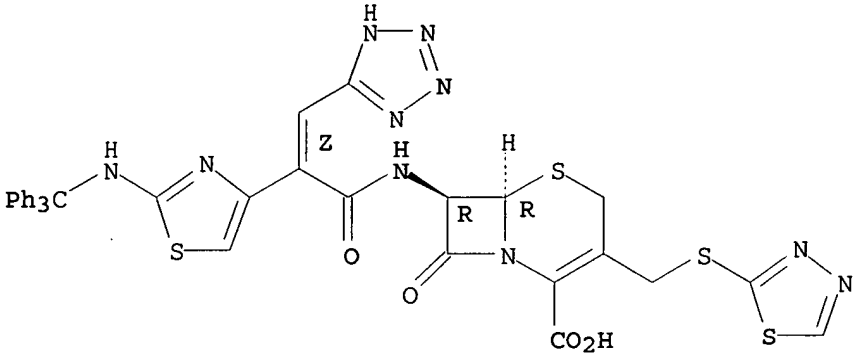
I

AB The title compds. I [R1 = (protected) CO2H, CO2-; R3 = (protected) amino; Y = H, halo; one of W and X is H, the other is Me, MeSCH2, cycloalkyl, pyrazolyl, tetrazolyl, 2-oxodihydropyridyl, etc.; R2 = pyridino, thiazolylthio, alkyl-substituted tetrazolylthio; with the proviso that Y is halo when one of W and X is H and the other is Me; when R1 = CO2-, R2 is pyridinio], useful as antibiotics (no data), were prepared Condensation of 1-(2-tert-butoxycarbonylamino-5-chlorothiazol-4-yl)-1-(Z)-propenecarboxylic acid (preparation given) with 7-amino-3-pyridiniummethyl-3-cephem-4-carboxylic acid-2HCl, followed by deprotection in PhOMe/CF3CO2H gave 7-[1-(2-amino-5-chlorothiazol-4-yl)]-1-(Z)-propenecarboxamido-3-pyridiniummethyl-3-cephem-4-carboxylate.

IC ICM C07D501-24
ICA A61K031-545
CC 26-5 (Biomolecules and Their Synthetic Analogs)
Section cross-reference(s): 1
ST cephemcarboxylate alkenylcarboxamido prepn antibiotic; antibiotic alkenylcarboxamidocephemcarboxylate prepn
IT 24209-43-6 53090-86-1 96752-43-1
RL: RCT (Reactant); RACT (Reactant or reagent)
(acylation of)
IT 86978-22-5
RL: RCT (Reactant); RACT (Reactant or reagent)
(esterification and chlorination of)
IT 114569-41-4P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and acetylation of)
IT 110630-16-5P 110630-17-6P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and amidation of)
IT 114569-39-0P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation and conversion of, to (dimethylaminomethylene)aminothiazole

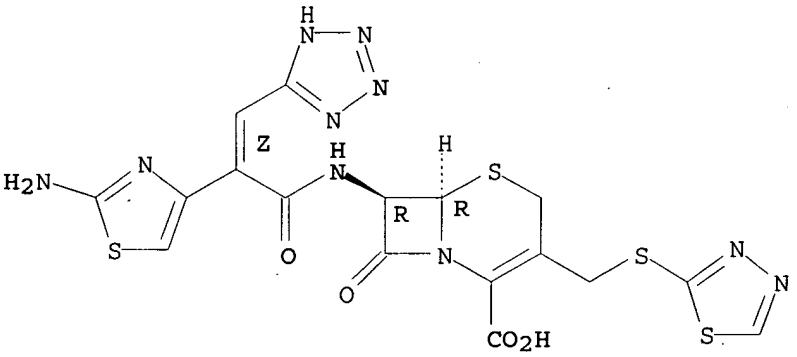
derivative)
IT 114569-42-5P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation and conversion of, to formamidothiazole derivative)
IT 114587-56-3P 114587-57-4P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and deprotection of)
IT 114569-40-3P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and reaction of, with methylthioacetaldehyde)
IT 110630-26-7P 114569-38-9P 114569-52-7P 114569-55-0P 114569-57-2P
114569-67-4P 114569-80-1P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation of, as antibiotic)
IT 114569-35-6P 114569-36-7P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of, as antibiotic intermediate)
IT 114569-43-6P 114569-44-7P 114569-45-8P 114569-46-9P 114569-47-0P
114569-48-1P 114569-49-2P 114569-50-5P 114569-51-6P 114569-53-8P
114569-54-9P 114569-56-1P 114569-58-3P 114569-59-4P 114569-60-7P
114569-61-8P 114569-62-9P 114569-63-0P 114569-64-1P 114569-65-2P
114569-66-3P 114569-68-5P 114569-69-6P 114569-70-9P 114569-71-0P
114569-72-1P 114569-73-2P 114569-74-3P 114569-75-4P
114569-76-5P 114569-77-6P 114569-78-7P 114569-79-8P
114569-82-3P 114569-83-4P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of, as cephalosporin antibiotic intermediate)
IT 55408-11-2, 5-Chloromethyl-1H-tetrazole 68363-43-9 87288-57-1
114569-81-2
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, in preparation of cephalosporin antibiotic intermediate)
IT 11111-12-9P
RL: SPN (Synthetic preparation); PREP (Preparation)
(thiazolyl, preparation of, as anntibacterials)
IT **114569-76-5P 114569-77-6P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of, as cephalosporin antibiotic intermediate)
RN 114569-76-5 HCAPLUS
CN 5-Thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylic acid, 8-oxo-7-[[1-oxo-3-(1H-tetrazol-5-yl)-2-[2-[(triphenylmethyl)amino]-4-thiazolyl]-2-propenyl]amino]-3-[(1,3,4-thiadiazol-2-ylthio)methyl]-, [6R-[6α,7β(Z)]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



RN 114569-77-6 HCAPLUS
CN 5-Thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylic acid, 7-[[2-(2-amino-4-thiazolyl)-1-oxo-3-(1H-tetrazol-5-yl)-2-propenyl]amino]-8-oxo-3-[(1,3,4-thiadiazol-2-ylthio)methyl]-, [6R-[6α,7β(Z)]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



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